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10/561,570	09/11/2007	**Shinichi Watanabe**	11582-016-999	5811

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/561,570	WATANABE ET AL.	
	Examiner	Art Unit	
	Thaian N. Ton	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 January 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10-13,16-23 and 25-40* is/are pending in the application.

4a) Of the above claim(s) *4,6-8,10-13,16-23,25,26 and 35-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5 and 27-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants Amendment and Remarks, filed 1/27/10, have been entered. Claims 1-8, 10-13, 16-23, 25-40 are pending; claim 1 is amended; claims 27-40 are newly added; claims 4, 6-8, 10-13, 16-23, 25, 26, 35-40 are withdrawn; claims 1-3, 5, 27-34 are under current examination.

Priority

Acknowledgment is made of applicant's claim for priority based on PCT/EP2004/006474. It is noted, however, that applicant has not filed a certified copy of the PCT/EP2004/006474 application as required.

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-3 and 5) in the reply filed on 7/24/09 is acknowledged.

The restriction requirement is still deemed proper and is therefore made FINAL.

Claims 4, 6-8, 10-13, 16-23, 25 and 26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected groups, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 7/24/09.

Newly Added Claims 35-40

Newly submitted claims 35-40 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the newly added claims are directed to isolated antibodies that specifically bind a RC kinase polypeptide. Antibodies are distinct in structure and function than the elected

polynucleotide. Additionally, antibodies can be used for distinct purposes, such as immunological assays.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 35-40 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 5 and newly added claims 27-34 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

An isolated polynucleotide sequence encoding an RC kinase polypeptide, being selected from the group consisting of:

a) a polynucleotide encoding a RC Kinase polypeptide comprising an amino acid sequence selected from the group consisting of: amino acid sequences which are at least 90% (or 96% or 100%) identical to the amino acid sequence shown in SEQ ID NO: 10; and the amino acid sequence shown in SEQ ID NO: 10;

b) a polynucleotide comprising (or consisting of) the sequence of SEQ ID NO: 4;

c) a polynucleotide the sequence of which deviates from the polynucleotide sequences specified in (a) or (b) due to the degeneration of the genetic code.

The specification is additionally enabling for expression vectors and host cells comprising the polynucleotides recited above and method for producing an RC kinase polypeptide wherein the method comprises a) culturing the host cells under

conditions suitable for the expression of the RC kinase polypeptide and b) recovering the RC kinase polypeptide from the host cell culture.

The specification does not reasonably provide enablement for the breadth of the claims which encompass polynucleotides which hybridizes under stringent conditions to a polynucleotide specified in (a) and (b), above. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Applicants' Arguments. Applicants argue that no undue experimentation is required to make or use the claimed invention. Applicants argue that the test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, so long as it is routine. Applicants argue that the Patent Office has stated that assays and techniques used to make and use variants of the polynucleotides of SEQ ID NO: 4 or the polypeptide of SEQ ID NO: 10 having the recited structural characteristics are well-known in the art, but that the number of species encompassed by the claims is extremely large, and thus the spec must provide a reasonable amount of guidance with respect to the direction in which experimentation should proceed so that a reasonable number of species can be selected for testing, and this guidance is lacking (p.12 of the Response). Applicants argue that claim 1 has now been amended to recite that the amino acid sequences are at least 90% identical to the amino acid sequence shown in SEQ ID NO: 10, and

that the phrase that encompasses Applicants argue that this represents a reasonable number of species of the presently claimed polynucleotides.

Applicants further argue that the specification discloses variants and homologs of the disclosed RC kinase polynucleotides that can be identified by hybridization of candidate nucleotides to known RC kinase polynucleotides under stringent conditions, or screened from cDNA expression libraries. Also, Applicants argue that the specification discloses that stringent conditions can be used to obtain variants encoding a RC kinase polypeptide that are at least 90% identical to SEQ ID NO: 10, for example by using specific wash conditions (p. 13, ¶1-2).

Applicants argue that the specification provides a working example which shows that RC kinase activity of a candidate polypeptide can routinely be screened by detection of its phosphorylation of other known RC kinase polypeptides, such as MKK4 and MKK6. Applicants argue that taken with the disclosure, the specification provides a reasonable amount of guidance with respect to testing and making a reasonable number of species of polynucleotides encoding a RC kinase polypeptide comprising amino acid sequences which are at least 90% identical to SEQ ID NO: 10, polynucleotides that hybridize under stringent conditions to such polynucleotides, and polynucleotides wherein the sequence of which deviates from such polynucleotides sequence. See pages 13-14 of the Response.

Response to Arguments. These arguments have been considered and are partially persuasive, with regard to polynucleotides that encode a RC kinase polypeptide that comprise amino acid sequences that are 90% identical to SEQ ID NO: 10, as well as polynucleotides that comprise the sequence of SEQ ID NO: 4, and polynucleotides wherein the sequence deviates from the polynucleotide sequences specified in a) or b) (see above scope of enablement). The arguments are not persuasive with regard to:

1. part c) of claims 1, 27 and 31; part and additionally,

2. part d) of claims 1, 27 and 31 which recites that the polynucleotide deviates from the nucleotide sequences specified in a) to c) due to degeneration of the genetic code. In particular, the Examiner has determined that the scope of enablement, with regard to part d) of claims 1, 27, 31 is with regard to step a) or (not and) b). That is, the polynucleotide does not differ from the combined polynucleotides recited in a) and b) of claim 1.

With regard to identification of homologs or variants by hybridization, the specification provides guidance for specific conditions, which are not instantly claims. That is, Applicants are arguing limitations that are not found within the instant claims. The claims encompass any type of stringent conditions – which are not specifically and uniquely defined by the claims – and encompass any length of polynucleotide that hybridizes to any portion of SEQ ID NO: 4. For example, the claims do not recite that the polynucleotide claimed in claim 1, part c) or the polynucleotide claimed in claim 31, part c) hybridizes to the full length SEQ ID NO: 4. Thus, these embodiments continue to read on fragments of SEQ ID NO 4.

Neither art nor the specification provides any teaching or guidance as to (1) which nucleotides in the polynucleotide of SEQ ID NO: 4 can be modified and which ones are conserved such that one of skill in the art can make variants as recited encoding polypeptides with the same biological activity as that of the polypeptide of SEQ ID NO: 10, (2) which segments of the polypeptide of SEQ ID NO: 10, or the polynucleotide of SEQ ID NO: 4, are essential for activity, other than the conserved kinase domain, and (3) the general tolerance of RC kinases to structural modifications and the extent of such tolerance. The art clearly teaches that changes in a protein's amino acid sequence to obtain the desired activity without any guidance/knowledge as to which amino acids in a protein are required for that activity is highly unpredictable. At the time of the invention there was a high level of unpredictability associated with altering a polypeptide sequence with an expectation that the polypeptide will maintain the desired activity.

Therefore, taking into consideration the extremely broad scope of the claims, the lack of guidance, the amount of information provided, the lack of knowledge about a correlation between structure and function, the high degree of unpredictability of the prior art in regard to structural changes and their effect on function, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to practice the claimed invention. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

Written Description

Claims 1-3, 5 and newly added claims 27-34 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that, "[A]pplicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." *Vas-Cath Inc. v. Mahurkar,* 19USPQ2d at 1117. The specification does not, "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." *Vas-cath Inc. v. Mahurkar*, 19USPQ2d at 1116.

Applicants' Arguments. Applicants argue that the claims satisfy the written description requirement because the claims have now been amended to delete the phrase "fragment, derivative or allelic variation of a polynucleotide sequence specified in a) to d)". Applicants submit that the rejection with regard to "fragments

or derivatives" is obviated by amendments to claim 1. Applicants submit that reciting that the amino acid sequences are at least 90% identical to the amino acid sequence shown in SEQ ID NO: 10 have adequate written description by the specification. Applicants submit that the specification provides adequate description as to the common identifying characteristics of the claimed polynucleotides, in addition to the sequences of certain polynucleotide species. Applicants argue that the specification discloses structural elements that are common among the species of the claimed genus of polynucleotides that encode a RC kinase. Apps argue that the specification discloses that biologically active variants, such as SEQ ID NOS 1-6 retain a RC kinase activity despite the absence of certain exons or portions of certain exons, and that the specification provides guidance to which structural regions of a RC kinase are amenable to sequence variation without losing the biological property of a RC kinase, and thus, 100% homology to SEQ ID NO: 4, or a polynucleotide encoding SEQ ID NO: 10 is not required to retain RC kinase activity. See pages 16-17 of the Response.

Applicants argue that with regard to the breadth of the genus of polynucleotides that hybridize to SEQ ID NO: 4, Applicants submit that claim 1 meets the written description guidelines because it recites that the polynucleotide which hybridizes under stringent conditions to a polynucleotide specified in a) and b), and in the *Written Description Guidelines*, the Office has provided an example of genus claims to nucleic acids based upon their hybridization properties and has determined that such claims may adequately be described if they hybridize under highly stringent conditions to known sequences because such conditions dictate that all species within the genus will be structurally similar. Applicants argue that the genus of polynucleotides in claim 1 fully meets the written description requirement. See page 18 of the Response.

Response to Arguments. These arguments are found to be partially persuasive, with regard to claims 1, 27 and 31 parts a)–b), and part d) as it relates

to parts a) and b). However, the arguments are not persuasive with regard to claims 1, 27, and 31, part c). In particular, the claims do not recite that the polynucleotide that hybridizes to the polynucleotide in parts a) and b), hybridizes to the full length sequence of SEQ ID NO: 4, for example. Thus, the claims continue to encompass variants that would encode for a functional RC kinase polypeptide.

Turning to the *Written Description Guidelines*, the Examiner notes that the instant claims are most similar to the Example 6 (page 22). Claim 3 of the example recites that the nucleic acid binds to the complement of the sequence it hybridizes to. In the instant case, Applicants' sequence binds to the polynucleotide itself, which not yield an encoded protein. In the instant case, Applicants disclose the reduction to practice of a single species of the claimed genus (*i.e.*, SEQ ID NO: 4), but the specification does not indicate any nucleic acids that both hybridize to the complement of SEQ ID NO: 4 and encode an RC kinase polypeptide. The citation that Applicants recite discusses hybridization under *highly* stringent conditions, whereas the instant claims recite *stringent* conditions, thus, the scope of the instant claims is far broader than *highly* stringent conditions. Given that the claims encompass a vast number of variants, that the specific hybridization conditions are not provided nor specifically and uniquely defined in the claims or the specification, the polynucleotides encompassed by claims 1, 27 and 31, part d) are not described. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

The claims encompass an extremely large genus of nucleic acids which are structurally or functionally unrelated. A sufficient written description of a genus of nucleic acids may be achieved by a recitation of a representative number of nucleic

acids defined by their nucleotide sequence or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. However, in the instant case, either (1) there is no structural feature which is representative of all the members of the genus of nucleic acids recited in the claims, or (2) the structural features recited/interpreted, such as "a polynucleotide hybridizing under stringent conditions", do not constitute a substantial portion of the genus as the remainder of any nucleic acid encoding/comprising said structural elements is completely undefined and the specification does not define the remaining structural features for members of the genus to be selected.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGFs were found to be unpatentable due to lack of written description for that broad class. The specification only provided the bovine sequence.

Applicant is reminded that *Vas-Cath* makes clear that the written description of 35 U.S.C. 112 is severable from its enablement provision [see p. 1115].

Claim Rejections - 35 USC § 112

The prior rejection of claims 1-3 and 5 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of Applicants' amendment to the claims which longer recite the phrase, "at least about".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 and 5 and newly added claims 27-34 stand rejected under 35 U.S.C. 102(b) as being anticipated by WO 02/090525 A2 (published November 14, 2002).

Applicants' Arguments. Applicants argue that the claims have now been amended to recite amino acid sequences that are at least 90% identical to the amino acid sequence shown in SEQ ID NO: 10, and that the '525 publication fails to each and every element of independent claim 1, because the '525 publication does not teach a polynucleotide encoding an RC kinase polypeptide that is at least 90% identical to the amino acid sequence shown in SEQ ID NO: 10, and does not teach a polynucleotide that hybridizes under stringent conditions to such nucleotides. See page 19 of the Response.

Response to Arguments. These arguments have been considered, but are not persuasive. It is noted that claims 1, 27 and 31, part c) recite polynucleotides that hybridize under stringent conditions to polynucleotides specified in parts a) and b). There is no recitation that the polynucleotide in part c) hybridizes to the full length polynucleotides in parts a)-b). Thus, because the '525 publication teaches 88.2% similarity to SEQ ID NO: 10, and polynucleotides that hybridize to this sequence, the '525 fulfills the limitations of the claims by providing a polynucleotide that hybridizes to a polynucleotide specified in a)-b).

Rejection

Regarding claims 1, 27 and 31 the '525 document teaches SEQ ID NO: 2, which encodes a polynucleotide that is 88.2% identical to SEQ ID NO: 10 (see

attached alignment) and is 76.4% identical to SEQ ID NO: 4 (see attached alignment). The '525 document teaches that these amino acid sequences encode human kinase peptides and proteins that are related to the MEK kinase alpha subfamily (see p. 5, lines 21-24). The '525 document teaches nucleic acids that can hybridize to the polynucleotides (p. 29, lines 13+).

Regarding claims 2, 28, 32, the '525 document teaches that the nucleic acids encoding the kinase peptides can be isolated (p. 26, lines 10+) and can be contained in an expression vector (p. 26, lines 25-26; p. 30, lines 19-24).

Regarding claims 3, 29, 33, the '525 document teaches that the nucleic acids encoding the kinase peptides can be maintained in a host cell (p. 26, lines 26-27; p. 31, lines 3-4).

Regarding claims 5, 30, 34, the '525 document teaches that the isolated kinase peptides can be purified from cells that have been altered to express it recombinantly (p. 8, lines 17-18).

Accordingly, the '525 document anticipates the claims.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thaian N. Ton whose telephone number is (571)272-0736. The examiner can normally be reached on 9-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Thaian N. Ton/
Primary Examiner, Art Unit 1632